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Note

Stereospecific synthesis of (−)-*allo*-muscarine from D-glucose

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(−)-*allo*-Muscarine (**1**) is a C-2 epimer of (+)-muscarine which also occurs in *Amanita muscaria* [1] and shows similar biological activity [2] as (+)-muscarine itself. Several non-carbohydrate based syntheses of **1** have already been reported [3–6], as well as a non-stereospecific one achieved from 2-deoxy-L-*erythro*-pentose [7]. In the course of our studies related to preparation of optically pure muscarine stereoisomers by chirality transfer from monosaccharides, a novel synthesis of (+)-*epiallo*-muscarine from D-glucose has already been completed [8]. We report now the first stereospecific synthesis of (−)-*allo*-muscarine (**1**) based on D-glucose as a chiral precursor.

The 2,5-anhydro-L-idose derivative **2**, readily available from D-glucose [8], was used as a starting material in this work. Treatment of **2** with mesyl chloride in pyridine at 4 °C gave the expected trimesylate **3** in a yield of 94%. Reaction of **2** with tosyl chloride in pyridine at room temperature gave an 86% yield of the corresponding 4-*O*-tosyl derivative **4**. Both trisulfonates **3** and **4** reacted smoothly with sodium hydrogensulfide in *N*,*N*-dimethylformamide at 80 °C to afford the corresponding bicyclic oxathiane derivatives **5** and **6** in 58 and 90% yield, respectively. The similar inter- and intramolecular S_N2 process also represents one of the key steps in the reported synthesis of (+)-*epiallo*-muscarine from D-glucose [8]. Raney nickel desulfurization of **5** in ethanol for 24 h at room temperature afforded the corresponding 3,6-dideoxy derivative **7** in a yield of only 24%. TLC (1:4 cyclohexane–ether) indicated that the product **7** (R_f 0.21)

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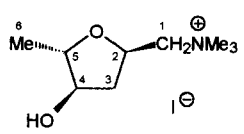
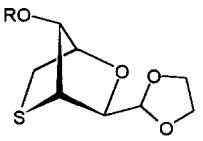
in the reaction mixture had been accompanied by at least an equal amount of an additional less-polar component (R_f 0.67). Although this material was chromatographically homogeneous in different solvent systems it appeared to be a mixture of two 2,5-anhydro-3,4,6-trideoxy derivatives in approximately 3:5 ratio as established by ^{1}H NMR integration of the anomeric proton signals (δ 4.79 and 4.83). However, when the 4-*O*-tosyl derivative **6** reacted under the same conditions, the desired 3,6-dideoxy derivative **8** was obtained in an acceptable yield of 50%. Both 4-sulfonates **7** and **8** reacted readily with potassium benzoate in *N*,*N*-dimethylformamide at 100 °C to afford the chiral synthon **9** (54 and 59%, respectively) with all chiral centres corresponding to (−)-*allo*-muscarine (**1**).

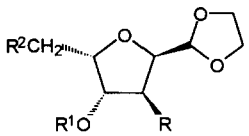


(-)-*allo*-Muscarine iodide (**1**)



5 R = Ms

6 R = Ts



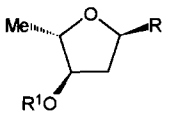
2 R = R^2 = OMs; R^1 = H

3 R = R^2 = OMs; R^1 = Ms

4 R = R^2 = OMs; R^1 = Ts

7 R = R^2 = H; R^1 = Ms

8 R = R^2 = H; R^1 = Ts



9 R =  ; R^1 = Bz

10 R = CHO; R^1 = Bz

11 R = CH(OH)$_2$; R^1 = Bz

12 R = CH$_2$OH; R^1 = Bz

13 R = CH$_2$I; R^1 = Bz

14 R = CH$_2$NMe$_2$; R^1 = H

Hydrolytic removal of the dioxolane protective group in **9** was achieved with a mixture of trifluoroacetic acid and aq hydrochloric acid at 4 °C. The product had a low mobility in TLC (R_f 0.25; 4:1 toluene–acetone) suggesting that it predominantly existed in the *gem*-diol form **11** rather than as the free aldehyde **10**. Due to its instability [1] it was not characterized further but was immediately reduced with sodium borohydride in methanol for 1 h at room temperature, to afford the corresponding primary alcohol **12** (52% from **9**). Reaction of **12** with iodine, imidazole, and triphenylphosphine in refluxing toluene for 2 h afforded the known [5] iodo derivative **13** in 81% yield.

[1] Compound **11** decomposed slowly on standing to give a variety of products.

Table 1
NMR data for **1** (in D_2O)

	Chemical shift (δ) and *J* (Hz)							
	H-1a	H-1b	H-2	H-3a	H-3b	H-4	H-5	H-6
This work	3.42	3.60	4.65	1.63	2.58	4.05	4.04	1.18
Ref. [5]	3.34	3.58	4.63	1.56	2.51	3.97	3.96	1.11
	$J_{1a,1b}$	$J_{1a,2}$	$J_{1b,2}$	$J_{2,3a}$	$J_{2,3b}$	$J_{3a,4}$	$J_{3b,4}$	$J_{4,5}$
This work	13.9	1.0	10.3	5.9	8.3	5.1	6.1	4.0
Ref. [5]	14.0	1.3	9.8	5.8	8.0	5.4	6.0	4.1
	C-1	C-2	C-3	C-4	C-5	C-6	NMe_3	
This work	72.58	74.16	40.46	78.15	84.63	20.41	56.92	
Ref. [5]	72.37	74.03	40.22	77.95	84.51	20.22	56.66	

Treatment of **13** with dimethylamine in ethanol at 80 °C followed by subsequent *O*-debenzoylation gave (−)-*allo*-normuscarine (**14**) in a yield of 53%. Compound **14** was finally converted into (−)-*allo*-muscarine iodide (**1**) according to the reported procedure [5]. The ^1H and ^{13}C NMR data (Table 1) as well as physical constants of **1** thus obtained were in good agreement with those already reported [5].

1. Experimental

General methods.—Melting points were determined on a Büchi SMP 20 apparatus and were not corrected. Optical rotations were measured on an automatic polarimeter Polamat A (Zeiss, Jena). NMR spectra were recorded on a Bruker AC 250 E instrument, and chemical shifts are expressed in ppm downfield from tetramethylsilane. Mass spectra were recorded on a Kratos MS25 (low resolution) and Kratos MS9/50 (high resolution) instrument. TLC was performed on DC Alufolien Kieselgel 60 F_{254} (Merck) with 4:1 (*A*), 19:1 (*B*), 49:1 (*C*) CH_2Cl_2–acetone, 4:1 toluene–acetone (*D*), di-isopropyl ether (*E*), and 4:1 $CHCl_3$–MeOH (*F*). Column chromatography was carried out using Kieselgel 60 (under 0.063 mm; Merck). Flash column chromatography was performed using ICN silica 32–63. All organic extracts were dried with anhydrous Na_2SO_4. Organic solutions were concentrated in a rotary evaporator under diminished pressure at a bath temperature below 35 °C.

*2,5-Anhydro-3,4,6-tri-*O*-methanesulfonyl-*L*-idose ethylene acetal* (**3**).—To a stirred and ice-cooled solution of dimesylate **2** [8] (5 g, 13.88 mmol) in dry pyridine (35 mL) was added mesyl chloride (2.5 mL, 32.25 mmol). The mixture was stored at 4 °C for 48 h, then poured into cold water. The precipitate was collected, washed with water, and dried, to afford chromatographically pure **3** (5.74 g, 94%) as white solid; mp 178–180 °C. Recrystallized from MeOH, an analytical sample of **3** showed mp 184 °C and $[\alpha]_D$ −3.4° (*c* 1.0, $CHCl_3$); R_f 0.71 (*A*); ^1H NMR ($CDCl_3$): δ 3.18, 3.29, and 3.34 (3 s, each 3 H, 3 $MeSO_2$), 3.84–4.05 (m, 4 H, dioxolane), 4.23 (dd, 1 H, $J_{1,2}$ 5.7, $J_{2,3}$ 4.2

Hz, H-2), 4.38 (dd, 1 H, $J_{6a,6b}$ 11.1, $J_{5,6a}$ 6.9 Hz, H-6a), 4.47 (dd, 1 H, $J_{5,6b}$ 4.1 Hz, H-6b), 4.73 (dt, 1 H, $J_{4,5}$ 4.2 Hz, H-5), 5.1 (d, 1 H, H-1), 5.42 (dd, 1 H, $J_{3,4}$ 2.1 Hz, H-3), 5.47 (dd, 1 H, H-4); ^{13}C NMR ($CDCl_3$): δ 37.44, 38.22, and 38.25 (3 $MeSO_2$), 65.82 and 65.96 (2 CH_2, dioxolane), 68.4 (C-6), 78.16 (C-5), 80.04 (C-2), 82.2 (C-4), 82.58 (C-3), 102.34 (C-1). Mass spectrum: *m/z* 440.0039. Calcd for $C_{11}H_{20}O_{12}S_3$: 440.0117 (M^+).

*2,5-Anhydro-3,6-di-*O*-methanesulfonyl-4-*O*-p-toluenesulfonyl-*L*-idose ethylene acetal* (**4**).—To a solution of **2** (0.5 g, 7.07 mmol) in dry pyridine (10 mL) was added tosyl chloride (1.35 g, 7.07 mmol). The mixture was kept at room temperature for 6 days, then acidified with aq HCl (1:1, 30 mL), and extracted with CH_2Cl_2 (4 × 20 mL). The extracts were combined, washed with water and satd aq $NaHCO_3$, dried, and concentrated. Flash chromatography (19:1 CH_2Cl_2–EtOAc) of the residue (0.73 g) yielded pure **4** (0.612 g, 86%) as a white solid. Recrystallization from MeOH afforded an analytical sample of **4**, as colourless needles; mp 119 °C; $[\alpha]_D$ +25.1° (*c* 1.15, $CHCl_3$); R_f 0.37 (*D*); ^{1}H NMR ($CDCl_3$): δ 2.48 (s, 3 H, Me from Ts), 3.01 and 3.1 (2 s, each 3 H, 2 $MeSO_2$), 3.82–4.05 (m, 4 H, dioxolane), 4.17 (m, 2 H, H-2 and H-6), 4.34 (dd, 1 H, $J_{5,6b}$ 6, $J_{6a,6b}$ 10.7 Hz, H-6b), 4.57 (ddd, 1 H, $J_{4,5}$ 4.2, $J_{5,6a}$ 5.6 Hz, H-5), 5.08 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1), 5.1 (dd, 1 H, $J_{3,4}$ 2.1 Hz, H-4), 5.83 (dd, $J_{2,3}$ 4 Hz, H-3), 7.4–7.95 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.73 (Me from Ts), 37.57 and 37.93 (2 $MeSO_2$), 65.3 and 65.88 (2 CH_2, dioxolane), 77.15 (C-5), 79.28 (C-2), 80.78 (C-4), 81.34 (C-3), 101.36 (C-1), 128.37, 130.33, 131.3, and 146.2 (Ar). Anal. Calcd for $C_{17}H_{24}O_{12}S_3$: C, 39.53; H, 4.69; S, 18.59. Found: C, 39.68; H, 4.85; S, 18.31.

*2,5-Anhydro-4-*O*-methanesulfonyl-3,6-thioanhydro-*L*-talose ethylene acetal* (**5**).—To a solution of **3** (3.1 g, 7 mmol) in *N,N*-dimethylformamide (21 mL) was added NaSH monohydrate (4.1 g, 73 mmol). The mixture was stirred in an atmosphere of N_2 at 90 °C for 3 h, then poured into water (50 mL) and extracted with CH_2Cl_2 (3 × 40 mL). The combined extracts were washed with water, dried, and concentrated to a dark-brown syrup. Column chromatography (100 g, 99:1 CH_2Cl_2–acetone) of the residue (2 g) afforded pure **5** (1.14 g, 58%) as a pale-yellow syrup. Crystallization from MeOH gave an analytical sample of **5** as colourless needles; mp 92 °C; $[\alpha]_D$ −2.7° (*c* 1.25, $CHCl_3$); R_f 0.57 (*C*); ^{1}H NMR ($CDCl_3$): δ 3.0 (dd, 1 H, $J_{6a,6b}$ 11.1, $J_{5,6a}$ 1.2 Hz, H-6a), 3.07 (s, 3 H, $MeSO_2$), 3.08 (dd, 1 H, $J_{5,6b}$ 2 Hz, H-6b), 3.56 (d, 1 H, $J_{3,4}$ 2.4 Hz, H-3), 3.8–3.98 (m, 4 H, dioxolane), 4.25 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-2), 4.37 (m, 1 H, $J_{4,5}$ 3 Hz, H-5), 4.74 (d, 1 H, H-1), 5.42 (t, 1 H, H-4); ^{13}C NMR ($CDCl_3$): δ 34.67 (C-6), 38.41 ($MeSO_2$), 46.26 (C-3), 65.09 (2 CH_2, dioxolane), 76.22 (C-5), 77.91 (C-4), 88.26 (C-2), 102.03 (C-1). Anal. Calcd for $C_9H_{14}O_6S_2$: C, 38.29; H, 5.00; S, 22.67. Found: C, 38.09; H, 4.89; S, 22.52.

*2,5-Anhydro-3,6-thioanhydro-4-*O*-p-toluenesulfonyl-*L*-talose ethylene acetal* (**6**).—A suspension containing **4** (0.52 g, 1 mmol) and NaSH monohydrate (0.37 g, 5 mmol) in *N,N*-dimethylformamide (10 mL) was stirred in an atmosphere of N_2 at 80 °C for 24 h. The solvent was removed by distillation in high vacuum and the residue extracted with EtOAc (3 x 10 mL). The extracts were combined, filtered, and concentrated to a brown syrup. Flash chromatography (19:1 toluene–acetone) of the residue (0.45 g) afforded pure **6** (0.325 g, 90%) as a colourless syrup; $[\alpha]_D$ −4.6° (*c* 1.1, $CHCl_3$); R_f 0.67 (*D*); ^{1}H NMR ($CDCl_3$): δ 2.48 (s, 3 H, Me from Ts), 3.01 (dd, 1 H, $J_{6a,6b}$ 11, $J_{5,6a}$ 1.2 Hz,

H-6a), 3.06 (dd, 1 H, $J_{5,6b}$ 1.2 Hz, H-6b), 3.3 (d, $J_{3,4}$ 2.1 Hz, H-3), 3.84–3.98 (m, 4 H, dioxolane), 4.25 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-2), 4.47 (m, 1 H, $J_{4,5}$ 3 Hz, H-5), 4.73 (d, 1 H, H-1), 5.35 (t, 1 H, H-4), 7.36–7.86 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.7 (Me from Ts), 34.82 (C-6), 46.26 (C-3), 65.28 and 65.35 (2 CH_2, dioxolane), 76.38 (C-5), 78.7 (C-4), 88.4 (C-2), 128.06, 129.9, 133.0, and 145.37 (Ar).

*2,5-Anhydro-3,6-dideoxy-4-*O*-methanesulfonyl-*L-lyxo*-hexose ethylene acetal* (**7**).—A suspension of **5** (1.4 g, 4.96 mmol) and Raney Ni (14 mL) in EtOH (30 mL) was hydrogenated at room temperature and normal pressure of H_2 for 24 h. The mixture was filtered through a Celite pad and the catalyst was washed with 1:1 EtOH–EtOAc (80 mL). The filtrate and washings were combined and concentrated. The residue was treated with boiling CH_2Cl_2 (3 × 15 mL), then filtered, and the solvent evaporated. The residue (0.77 g) was purified by flash chromatography (di-isopropyl ether) to afford pure **7** (0.3 g, 24%) as white solid. Recrystallized from EtOH, **7** had mp 87 °C and $[\alpha]_D$ +20.2° (*c* 0.39); R_f 0.37 (*E*); ^{1}H NMR ($CDCl_3$): δ 1.29 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 2.28 (ddd, 1 H, $J_{3a,3b}$ 13.5, $J_{2,3a}$ 8, $J_{3a,4}$ 4.6 Hz, H-3a), 2.33 (ddd, 1 H, $J_{2,3b}$ 7.2, $J_{3b,4}$ 1.6 Hz, H-3b), 3.04 (s, 3 H, $MeSO_2$), 3.83–4.07 (m, 4 H, dioxolane), 4.2 (dd, 1 H, $J_{4,5}$ 3.4 Hz, H-5), 4.28 (ddd, 1 H, $J_{1,2}$ 3.6 Hz, H-2), 4.89 (d, 1 H, H-1), 5.13 (m, 1 H, H-4); ^{13}C NMR ($CDCl_3$): δ 14.6 (C-6), 34.2 (C-3), 38.44 ($MeSO_2$), 65.2 and 65.54 (2 CH_2, dioxolane), 77.12 (C-2), 77.66 (C-5), 82.4 (C-4), 104.24 (C-1). Mass spectrum: *m/z* 251 ($M^+ - 1$). Anal. Calcd for $C_9H_{16}O_6S$: C, 42.85; H, 6.39; S, 12.71. Found: C, 43.10; H, 6.51; S, 12.54.

*2,5-Anhydro-3,6-dideoxy-4-*O*-*p*-toluenesulfonyl-*L-lyxo*-hexose ethylene acetal* (**8**).—To a solution of **6** (0.55 g, 1.54 mmol) in EtOAc (5 mL) was added a suspension of Raney Ni (5 mL) in EtOH (20 mL). The mixture was hydrogenated at room temperature and normal pressure of H_2 for 24 h. After workup as described above, the remaining crude **8** (0.29 g) was purified by flash chromatography (49:1 toluene–acetone) to afford pure **8** (0.25 g, 50%) as a colourless syrup; $[\alpha]_D$ +12.6° (*c* 0.95, $CHCl_3$); R_f 0.51 (*D*); ^{1}H NMR ($CDCl_3$): δ 1.16 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 2.14 (m, 2 H, $J_{2,3a}$ 7.6, $J_{3a,4}$ 3, $J_{2,3b}$ 7.9, $J_{3b,4}$ 2.2 Hz, 2 H-3), 2.44 (s, 3 H, Me from Ts), 3.81–4.03 (m, 4 H, dioxolane), 4.11 (qd, 1 H, $J_{4,5}$ 3.4 Hz, H-5), 4.2 (td, 1 H, $J_{1,2}$ 3.7 Hz, H-2), 4.8 (d, 1 H, H-1), 4.94 (m, 1 H, H-4), 7.29–7.89 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$): δ 14.69 (C-6), 21.69 (Me from Ts), 33.94 (C-3), 65.26 and 65.59 (2 CH_2, dioxolane), 77.09 (C-2), 77.8 (C-5), 83.15 (C-4), 104.35 (C-1), 127.78, 129.94, 133.95, and 144.95 (Ar).

*2,5-Anhydro-4-*O*-benzoyl-3,6-dideoxy-*L-arabino*-hexose ethylene acetal* (**9**).—(*a*). To a solution of **7** (0.3 g, 1.19 mmol) in *N,N*-dimethylformamide (5 mL) was added potassium benzoate (0.8 g, 5 mmol). The suspension was stirred at 100 °C for 48 h, and the solvent was removed by high vacuum distillation. The residue was treated with CH_2Cl_2 (3 × 10 mL) and the combined extracts were filtered and evaporated to an oil. Column chromatography (30 g, 4:1 toluene–EtOAc) of the residue (0.33 g) afforded pure **9** (0.18 g, 54%) as a colourless oil.

(*b*) The tosylate **8** (0.197 g, 0.6 mmol) reacted with potassium benzoate (0.4 g, 2.5 mmol) under the same conditions as described above to give crude **9** as an oil. Purification by flash chromatography (4:1 toluene–EtOAc) afforded pure **9** (0.098 g, 59%) as a colourless oil; $[\alpha]_D$ −4.2° (*c* 2.84, $CHCl_3$); R_f 0.66 (*B*); ^{1}H NMR ($CDCl_3$): δ 1.29 (d, 3 H, $J_{5,6}$ 6.7 Hz, H-6), 2.15 (ddd, 1 H, $J_{3a,3b}$ 14, $J_{2,3a}$ 3.7, $J_{3a,4}$ 3.6 Hz,

H-3a), 2.61 (ddd, 1 H, $J_{2,3b}$ 7, $J_{3b,4}$ 6.8 Hz, H-3b), 3.86–4.07 (m, 4 H, dioxolane), 4.13 (ddd, 1 H, $J_{1,2}$ 5.4 Hz, H-2), 4.36 (m, 1 H, H-5), 5.0 (d, 1 H, H-1), 5.15 (ddd, 1 H, $J_{4,5}$ 3.4 Hz, H-4), 7.37–8.16 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$): δ 18.61 (C-6), 32.52 (C-3), 65.2 and 65.37 (2 CH_2, dioxolane), 77.91 (C-2), 79.3 (C-4), 80.01 (C-5), 104.54 (C-1), 128.33, 129.55, 129.83, and 133.09 (Ph), 166.11 (C=O). Mass spectrum: m/z 277 ($M^+ - 1$).

*2,5-Anhydro-4-*O*-benzoyl-3,6-dideoxy-*L-arabino*-hexitol* (**12**).—To a solution of **9** (0.25 g, 0.9 mmol) in CF_3CO_2H (2 mL) was added aq 6 M HCl (0.5 mL). The mixture was kept at 4 °C for 24 h and then concentrated in vacuo by co-distillation with toluene. The remaining crude mixture (0.35 g) was dissolved in MeOH (5 mL) and treated with $NaBH_4$ (0.08 g, 2.1 mmol). The mixture was stirred at room temperature for 24 h, then poured into satd aq NaCl (5 mL) and extracted with CH_2Cl_2 (4 × 5 mL). The extracts were combined, washed with brine, dried, and evaporated. Column chromatography (45 g, 4:1 toluene–acetone) of the residue (0.25 g) afforded pure **12** (0.11 g, 52%) as a colourless syrup; $[\alpha]_D$ −34.6° (*c* 1.13, $CHCl_3$); R_f 0.64 (*D*); ^{1}H NMR ($CDCl_3$): δ 1.31 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6), 1.98 (ddd, 1 H, $J_{3a,3b}$ 13.7, $J_{2,3a}$ 5.5, $J_{3a,4}$ 3.4 Hz, H-3a), 2.17 (bs, 1 H, OH), 2.55 (ddd, 1 H, $J_{2,3b}$ 8.1, $J_{3b,4}$ 6.9 Hz, H-3b), 3.71 (m, 2 H, H-1a and H-1b), 4.32 (m, 2 H, H-2 and H-5), 5.16 (m, 1 H, H-4), 7.4–8.09 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$): δ 18.62 (C-6), 33.04 (C-3), 64.93 (C-1), 77.91 (C-2), 79.73 (C-5), 79.81 (C-4), 128.49, 129.62, 129.92, and 133.24 (Ph), 166.22 (C=O).

*2,5-Anhydro-4-*O*-benzoyl-1,3,6-trideoxy-1-iodo-*L-arabino*-hexitol* (**13**).—To a solution of **12** (0.54 g, 2.28 mmol) in dry toluene (10 mL) were added successively imidazole (0.33 g, 4.81 mmol), Ph_3P (1.28 g, 4.85 mmol), and I_2 (1 g, 3.91 mmol). The mixture was refluxed while stirring for 2 h and then concentrated in vacuo. Column chromatography (110 g, toluene) of the residue gave pure **13** (0.64 g, 81%) as a colourless syrup; $[\alpha]_D$ +35.7° (*c* 1.1, $CHCl_3$); lit. [5] $[\alpha]_D$ +33.97° (*c* 0.942, $CHCl_3$); R_f 0.71 (*C*); ^{1}H NMR ($CDCl_3$): δ 1.31 (d, 1 H, $J_{5,6}$ 6.1 Hz, H-6), 2.15 (ddd, 1 H, $J_{3a,3b}$ 14, $J_{2,3a}$ 4.4, $J_{3a,4}$ 3 Hz, H-3a), 2.65 (ddd, 1 H, $J_{2,3b}$ 7.6, $J_{3b,4}$ 6.8 Hz, H-3b), 3.34 (dd, 1 H, $J_{1a,1b}$ 9.8, $J_{1a,2}$ 7.7 Hz, H-1a), 3.37 (dd, $J_{1b,2}$ 5.9 Hz, H-1b), 4.4 (m, 1 H, H-2), 4.41 (m, 1 H, H-5), 5.18 (m, 1 H, $J_{4,5}$ 2.9 Hz, H-4), 7.38–8.16 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$): δ 9.74 (C-1), 18.95 (C-6), 36.86 (C-3), 77.88 (C-2), 79.78 (C-4), 80.58 (C-5), 128.49, 129.58, 129.74, and 133.27 (Ph), 166.1 (C=O).

(−)-allo-Normuscarine (**14**).—A sealed tube charged with a solution of iodo derivative **13** (0.64 g, 1.85 mmol) in ethanolic 20% Me_2NH (50 mL) was heated at 80 °C for 24 h. To the reaction mixture was then added NaOH (0.1 g), and the solution was refluxed for an additional 45 min. The volatiles were removed in vacuo, and the residue was treated with aq 10% HCl (10 mL) and extracted with ether (4 × 10 mL). The aqueous layer was rendered alkaline with aq 30% NaOH to pH 9 and extracted with CH_2Cl_2 (4 × 10 mL). The extracts were combined and evaporated to a yellow oil. Flash chromatography (4:1 toluene–acetone) of the residue afforded pure **14** (0.154 g, 53%) as a pale-yellow oil; $[\alpha]_D$ −39.7° (*c* 0.86, EtOH); lit. [5] $[\alpha]_D$ −38.62° (*c* 0.85, EtOH); R_f 0.5 (*F*); ^{1}H NMR ($CDCl_3$): δ 1.05 (d, 1 H, $J_{5,6}$ 6.7 Hz, H-6), 1.71 (m, 1 H, $J_{3a,3b}$ 14, $J_{3a,4}$ < 1 Hz, H-3a), 2.31 (dd, $J_{1a,1b}$ 14, $J_{1a,2}$ 1.8 Hz, H-1a), 2.38 (s, 6 H, Me_2N), 2.44 (ddd, 1 H, $J_{2,3b}$ 9.8, $J_{3b,4}$ 5.2 Hz, H-3b), 2.62 (dd, 1 H, $J_{1b,2}$ 3 Hz, H-1b), 3.88 (d, 1 H, $J_{4,5}$ < 1 Hz, H-4), 4.17 (q, 1 H, H-5), 4.36 (m, 1 H, H-2); ^{13}C NMR ($CDCl_3$): δ

19.74 (C-6), 36.99 (C-3), 47.94 (Me_2N), 62.72 (C-1), 75.19 (C-4), 77.88 (C-2), 84.74 (C-5).

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